IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#18/Supp. Brief
L.E.
11-10-03

In re Application of:	
MICHELSON *et al.*	Art Unit: 3626
Appln. No.: 09/923,385	Examiner: A. G. Kalinowski
Filed: August 8, 2001	Atty. Docket: 16602.003
For: SYSTEMS AND METHODS FOR SELECTING AND RECRUITING INVESTIGATORS AND SUBJECTS FOR CLINICAL STUDIES	Confirmation No.: 2406

AMENDED APPELLANTS' BRIEF

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is an Appeal under 37 C.F.R. § 1.191 from the decision of the Examiner as set forth in the final Official Action dated June 3, 2003. In that Action, claims 1-15 and 121-128 were finally rejected.

A Notice of Appeal is filed herewith. Authorization to charge Appellant's Deposit Account No. 50-2387 for the statutory fee of $160.00, for filing the Notice of Appeal, and $160.00 for submitting an appeal brief is included in the accompanying transmittal letter. *This Brief is submitted in triplicate.*

1. Real Parties in Interest

The real parties in interest are Leslie D. Michelson, residing at 804 North Whittier Drive, Beverly Hills, California 90210; Leonard Rosenberg, residing at 735 Lippincott Avenue, Morrestown, New Jersey 08057; and Lance Converse, residing at 39 High Gate Lane, Blue Bell, Pennsylvania, 19422. Acurian, Inc., a Delaware corporation with offices at 2 Walnut Grove Drive, Suite 375, Horsham, PA 19044, is an assignee of rights in this application, and therefore a real party in interest.

2. Related Appeals and Interferences

Appellants are unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 2-15 and 129-151 are pending. Claims 1 and 16-128 have been cancelled without prejudice. Claims 2, 129, 138, 139, 140, 149, 150, and 151 are independent. Claims 2-15 and 129-151 stand finally rejected under 35 U.S.C. § 103(a). Appellants appeal all of the rejections of each of the claims.

4. Status of Amendments

The Amendment filed March 4, 2003, was entered by the Examiner in the Official Action mailed June 3, 2003.

5. Summary of Invention

The invention is directed to a novel, integrated on-line interactive forum that promotes the exchange of information among clinical study sponsors, clinical study investigators, and potential participants in the clinical study (i.e., study subjects). The invention includes novel systems and methods for exchanging information among sponsors, investigators, and potential study subjects and for recruiting, selecting and enrolling appropriate subjects for clinical studies. Prior art systems provided information regarding clinical studies to potential participants, but left those participants to their own devices to recruit for or enroll in the studies. Other prior systems provided automated enrollment in specific studies once a patient had been informed of the study and been judged by an investigator (i.e., a physician) to be appropriate. The present invention, however, provides a single, Web-based interface that provides information about various clinical trials, accepts enrollment information for those trials, automatically determines if the prospective patient is appropriate for the trials and then automatically notifies the patient if they are an appropriate participant for a study. Through this novel, integrated approach, significant efficiencies are realized by bringing together sponsors, investigators and study subjects in one forum and by automatically evaluating and notifying prospective subjects.

6. Issues

The issues in this Appeal are:

(a) whether claims 2-5, 7-12 and 129 are unpatentable under 35 U.S.C. § 103(a) as being obvious over www.centerwatch.com (hereinafter CenterWatch) in view of Colon *et al.* (U.S. Patent No. 5,991,731);

(b) whether claims 3 and 130-137 are unpatentable under 35 U.S.C. § 103(a) as being obvious over CenterWatch in view of Colon *et al.* and further in view of "drkoop.com & Quintiles Launch service to recruit Clinical Trial Patients on the Internet" (hereinafter drkoop);

(c) whether claims 138-151 are unpatentable under 35 U.S.C. § 103(a) as being obvious over CenterWatch in view of Colon *et al.* and further in view of drkoop;

(d) whether claim 6 is unpatentable under 35 U.S.C. § 103(a) as being obvious over CenterWatch in view of Colon *et al.* and further in view of "Pharmaceutical industry Embraces Clinmark Dotcom" (hereinafter Clinmark);

(e) whether claims 13 and 14 are unpatentable over 35 U.S.C. § 103(a) as being obvious over CenterWatch in view of Colon *et al.* and further in view of Clinmark; and

(f) whether claim 15 is unpatentable over 35 U.S.C. § 103(a) as being obvious over CenterWatch in view of Colon *et al.* and further in view of Larkin, Marilynn, "Where to find clinical trials on the Web" (hereinafter Larkin).

7. Grouping of Claims

Claims 2-15 and 129-151 remain in this case. Claims 1, 129, 138, 139, 140, 149, 150, and 151 are independent. All of the claims at issue do not stand or fall together. Claim 2, 5, and 7-12 stand or fall together and are separately patentable from the other claims at issue. Claim 3 stands or falls alone and is separately patentable from the other claims at issue. Claim 4 stands or falls alone and is separately patentable from the other claims at issue. Claim 129 stands or falls alone and is separately patentable from the other claims at issue. Claims 130-151 stand or fall together and are separately patentable from the other claims at issue. Claim 6 stands or falls alone and is separately patentable from the other claims at issue. Claims 13 and 14 stand or fall

together and are separately patentable from the other claims at issue. Claim 15 stands or falls alone and is separately patentable from the other claims at issue. An explanation as to why the claims of each group are separately patentable is provided in section 8 below.

8. The Rejections and Prior Art of Record

A. The Rejection of Claims 2-5, 7-12 and 129 Under 35 U.S.C. § 103(a)

(i) *The Examiner's Rationale*

Claims 2-5, 7-12 and 129 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over CenterWatch in view of Colon *et al.*

In the Official Action mailed December 4, 2002, the Examiner acknowledged that CenterWatch does not explicitly disclose several steps of independent claim 2 including allowing a person or caregiver to register with a database, automatically presenting a questionnaire associated with the given clinical study to the person or caregiver, and storing answers submitted by the person or caregiver in the database. However, the Examiner asserted that Colon *et al.* disclosed each of the missing steps, and that it would be obvious to combine CenterWatch with Colon *et al.* to arrive at the invention of claim 2 (and dependent claims 3-5 and 7-12). *See* page 5, line 7, to page 6, line 4, of the Official Action mailed December 4, 2002.

In reply thereto, Appellants filed a Response, whereby the errors in the Examiner's rejection were discussed. The Appellants also added new claims 129-151.

In the final Official Action mailed June 3, 2003, the Examiner maintained the rejection of claims 2-5 and 7-12, and added new claim 129 to the rejection. The Examiner acknowledged that CenterWatch does not explicitly disclose several steps of independent claim 129, including allowing the person or caregiver to register with a database (*see* page 19, lines 5-6, of the final Official Action). However, the Examiner asserted that Colon *et al.* disclosed the missing step, and that it would be obvious to combine CenterWatch with Colon *et al.* to arrive at the invention of claim 129 (*see* page 19, lines 7-15, of the final Official Action).

(ii) *Summary of Appellants Position*

The Examiner has incorrectly relied on a statement in the summary of invention portion of Colon *et al.* for an alleged motivation to combine Colon *et al* and CenterWatch. In fact, no

such motivation to combine exists. Colon *et al.* disclose a database that receives information about a patient submitted by an investigator involved in a clinical trial. Once the investigator determines that the patient is appropriate for the study, the investigator enters the information into the system and thereby enrolls the patient in the trial. The system then randomly assigns a treatment (*e.g.*, drug A, drug B, placebo, etc.).

In contrast, CenterWatch is set up to inform a patient afflicted with a particular disease about clinical trials relating to the disease and drugs approved by the FDA for treatment of that disease. CenterWatch, however, is little more than a "clinical trials bulletin board," providing neither enrollment nor randomization assistance. Once the patient has obtained information concerning a trial of interest, it is up to the patient to contact the necessary people (*i.e.* the clinical trial investigator or sponsor) and enroll in the trial.

According to the Examiner, the following statement found in Colon's summary of the invention would have motivated the combination of these two very different systems:

> The system is particularly useful for large clinical studies of new drugs in determining patient eligibility, randomization and prescriptions online, while the patient is available in a physician's office.
>
> In a detailed particular embodiment, the system handles automatic assignment and randomization of thousands of participants in a clinical study with respect to care strategies to be administered to the study participants.

Column 1, ll 42-51, of Colon *et al.*

All of these uses, however, are for placing a patient who has presented in a physician's office into a specific clinical arm of a study. Nothing in this passage suggests that the system of Colon *et al.* could be extended to make a patient aware of a study, to provide information about various different types of trials directly to the patient, or to permit the patient to enter his or her own enrollment information and then be automatically evaluated and notified of the result of that evaluation. Indeed, by this very statement the system of Colon *et al.* is set in the doctor's office, with the doctor entering the enrollment information, making the enrollment determination and notifying the patient of enrollment. Colon *et al.* may be a system that assists a clinical investigator working in a large clinical study who has an appropriate study subject sitting in his

office, but it says nothing of bringing together potential study subjects, investigators and sponsors in the first place through an automated, Web-based forum. In fact, it would be unthinkable to one skilled in the art to do so, for to do so would violate the physican's obligation of confidentiality to the patient. If anything, these statements of Colon *et al.* teach away from the bulletin board approach of CenterWatch because there would be no use for a bulletin board system such as CenterWatch in a system like Colon *et al.* where the patient is already in the investigator's door.[1]

Moreover, CenterWatch and Colon *et al.* are concerned with two completely separate parts of the clinical trial process: (1) the identification of clinical trials of potential interest to patients (CenterWatch) and (2) the submission of information to the organization running the clinical trial for purposes of enrollment and randomization (Colon). The passage relied upon by the Examiner in Colon *et al.* says nothing about combining these two separate processes in a single automatic system. Rather, it expressly teaches the use of a computer input by the investigator "while the patient is available in a physician's office." Col. 1, ll. 46-47. This is an express teaching away from the concept of providing an automated, Web-based forum that patients can access themselves in the privacy of their own homes and be automatically enrolled in a study of interest. Thus, there is no motivation in either reference to combine those two distinct steps of the process.

The combination of CenterWatch and Colon *et al.* is also improper for yet the further reason that the database system of Colon *et al.* would be inoperable with the bulletin board system of CenterWatch, at least in the absence of significant modifications not suggested by the art before the Examiner. It is well-settled that an inoperable combination of prior art, far from suggesting the claimed invention, teaches away from that invention because those of ordinary skill in the art would simply not be motivated to create something that does not work. *In re: Gordon*, 733 F.2d 900 (Fed. Cir. 1984).

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[1] Nor does CenterWatch suggest a combination with Colon et al. CenterWatch provides a means for patients "seeking information about clinical trials" and who "would like to be notified by e-mail of future postings to this site in a particular therapeutic area." See the "Patient Notification Service" page on this web site. There is no suggestion that the patients could be signed up to the clinical trial using the site. CenterWatch just provides a means to get information out to patients regarding clinical trials they may be interested in – it is then up to the patient to contact the clinician/researcher in their geographical area to determine if they are eligible for the trial.

Colon *et al*'s database randomizes a number of participants who have already been clinically evaluated for a particular clinical study without revealing the randomization to either the patient or the administering physician. *See* column 2, ll 9-22, of Colon *et al.* CenterWatch, on the other hand, is intended to inform potential participants of available clinical studies, and enable them to begin a dialogue with the enrolling physician. *See* Patient Notification Service page of CenterWatch. Neither patients nor physicians are permitted to know for which arm of the study (study drug or placebo) the patient has been selected. Thus, in order to use the database techniques of Colon *et al.* in the system of CenterWatch one would need to modify those database techniques so that the users would not receive randomized clinical study information, as would necessarily occur in a Colon/CenterWatch combined system. The Examiner, of course, had no writing before him – other than Appellants' disclosure – that even arguably suggests such a modification. Certainly, the mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification itself. *In re: Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984).

Accordingly, the asserted combination of Colon *et al.* and CenterWatch is improper, as no motivation to combine those references has been shown to exist in the prior art. The Examiner's rejections based on that combination should therefore be reversed.

Furthermore, even if there were a motivation to combine CenterWatch and Colon *et al.*, and the combination were proper, Appellants submit that the combination does not render the pending claims unpatentable.

Claims 2-5 and 7-12 are directed towards a method for recruiting a person to participate in a clinical study comprising (a) presenting a website for the person to register with a database by providing registration and permission information; (b) registering the person with the database once registration and permission information is received; (c) automatically determining whether to provide the person with notice of a clinical study; (d) providing the person with notice of a clinical study; (e) automatically presenting a questionnaire associated with the clinical study to the person; and (f) storing the answers submitted by the person in the database. Claim 129 is directed to a method similar to the above, except steps (e) and (f) are replaced with a step that

allows for the person to amend their registration information in the database during a subsequent visit to the website.

Step (c) of claims 2-5 and 7-12 expressly recites:

> (c) after step (b), automatically determining, in accordance with the permission information and the registration information, whether to provide the person or caregiver with notice of a given clinical study associated with a disease condition of interest to the person.

Step (d) of claims 2-5 and 7-12 expressly recites:

> (d) providing the person or caregiver notice of the given clinical study only if a determination is made in step (c) to provide such notice.

Neither Colon *et al.* nor CenterWatch teach or suggest a method with such steps. As noted above, Colon *et al.* disclose a database that receives information about a patient submitted by an investigator involved in a clinical trial. Thus, the method of Colon *et al.* does not include a step of notifying a person of a given clinical study, because the person is obviously already aware of the study if they have presented themselves to an investigator involved in a clinical trial. CenterWatch provides nothing more than a clinical trials bulletin board, in which a person is notified of all clinical trials associated with their disease condition. In contrast, step (c) requires a determination as to whether to provide the person with information of "*a* given clinical study" and step (d) requires providing the person with "notice of *the* given clinical study," *i.e.*, the study for which an automatic determination was made pursuant to step (c). Thus, the claimed method includes notification of specific clinical trials most suitable for that person, not all clinical trials. Therefore, even if taken together, Colon *et al.* and CenterWatch do not disclose or suggest steps (c) or (d) of claims 2-5 and 7-12.

Claims 2-5 and 7-12 also expressly recite the step of:

> (e) automatically presenting a questionnaire associated with the given clinical study to the person or caregiver after step (d).

Note that the questionnaire recited here is "associated with *the* given clinical study," which is the study for which the automatic notice determination is made in step (c) of the claim. Thus, step (e) requires the automatic presentation not just of any questionnaire, but of one associated with the study for which it has been automatically determined that notice will be given.

Neither Colon *et al.* nor CenterWatch teach or suggest a method with such a step. In Colon *et al.*, while it is true that follow-up information can be entered into a database on a follow-up visit, *see* col. 7, l. 8 *et seq.*, the data fields into which such information is entered are not presented "automatically," as required by the claim. Quite the contrary, Colon *et al.* expressly states that the follow-up visit requires "starting up and initializing the system." Col. 7, l. 11, Figure 6, block 71. Similarly, CenterWatch provides no questionnaire, automatically or otherwise, after a notice determination is made. Thus, the asserted combination still does not meet all the elements of claim 2-5, and 7-12 and therefore would not have rendered them obvious.

Moreover, many of the claims that depend from claim 2 recite additional elements that distinguish them from the Examiner's combination. For example, claim 3 includes the following language:

> (g) Accessing the information stored along with other information in the database to determine whether the person qualifies to participate as a subject in a clinical study different from the given clinical study after step (f).

Neither CenterWatch nor Colon *et al.* says anything of accessing information already stored (e.g., earlier responses) to determine whether a person qualifies for a study different from the one they have already been given notice of (i.e., "different from *the* given study") and no suggestion has been asserted that would render such an additional step obvious.

Similarly, claim 4 includes a further refinement of the questionnaire:

> wherein the questionnaire includes criteria specific to a clinical study for determining whether the person is an eligible subject for the given clinical study.

The Examiner believed that this element was met by a passage from Colon *et al.* at col. 7, ll. 15-18. The Examiner, however, misquotes – and apparently misreads – that passage. According to the Examiner, the passage states that an application program performs "a test to see if the patient meets *a control parameter* for the study." Final Office Action at 6 (emphasis added). What the passage from Colon *et al.* actually says, however, is that the application program performs "a test to see if the patient meets *an 'in control' parameter* for the study." Col. 7, ll. 16-18 (internal quotation marks in original)(emphasis added). The Colon *et al.* patent goes on to explain that the determination of whether the patient meets the "in control" parameter determines whether the patient gets a "stepped prescription" or the normal prescription. Col. 7, ll. 18-26. Put differently, the Colon method involves determining whether a patient *already participating in the study* is within acceptable safety limits based on an already administered dosage of the study drug/placebo. Nothing in Colon *et al.* suggests that this parameter determines "whether the person is an eligible subject for the given clinical study," as required by claim 4. Indeed, the passage relied on by the Examiner is an explanation of Colon *et al*'s Figure 6, which describes a follow up visit to the physician's office after the patient has already been determined to be eligible for the study and enrolled. *Compare* col. 6, ll. 39-50. Thus, the Examiner has clearly erred.

Claim 129 was also rejected over this combination. With regards to steps (c) and (d) of claim 129, as noted above with respect to claims 2-5 and 7-12, neither Colon *et al.* nor CenterWatch disclose or suggest these steps. Furthermore, while claim 129 does not include the automatic presentation of a questionnaire after the notice determination, it does include the following step:

> (e) allowing the person or caregiver the opportunity to amend the registration information in the database during a subsequent visit to the web site.

Colon *et al.* says nothing of altering registration information during a subsequent visit. It permits the addition of new data and even the modification of the prescription during the initial enrollment process, column 2, ll 15-18, but that patent is silent on the later modification of registration information. Similarly, CenterWatch includes no such functionality. The closest is

comes is to permit a user to "un-subscribe" to the service. *See* Patient Notification Service page of CenterWatch. But that does not alter registration information, which would remain the same whether the user is enlisted in the service or not.

Accordingly, claims 2-5, 7-12, and 129 are not met by the combination of CenterWatch in view of Colon *et al.* and, even were there some motivation in the art to combine those references would not have rendered these claims obvious.

B. The rejection of Claims 3 and 130-137 Under 35 U.S.C. § 103(a)

(i) *The Examiner's Rationale*

Claims 3 and 130-137 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over CenterWatch in view of Colon *et al.* and further in view of drkoop.

In the final Official Action mailed June 3, 2003, the Examiner states that drkoop solves the deficiencies of CenterWatch and Colon *et al.*, as applied to claims 3 and 130-137, because drkoop purportedly discloses questionnaires which are pre-examination questionnaires, pre-screening questionnaires, screening questionnaires, screening questionnaires which are protocol specific, questionnaires designed for screening for clinically appropriate persons, and questionnaires that request information regarding inclusion/exclusion criteria, and assessing the answers to a questionnaire to determine whether the person qualifies to participate in a clinical study. Appellants respectfully disagree.

(ii) *Summary of Appellants Position*

As demonstrated above, there is no suggestion or motivation in the art to combine Colon *et al.* and CenterWatch. Thus, this rejection must fail for that reason alone. Moreover, there also is no motivation to further combine drkoop with Colon *et al.* and CenterWatch. Here, the Examiner is clearly using Appellants' disclosure as a template and merely picking and choosing references in the prior art, that have no connection to each other, in order to meet all the elements of the claims. Such hindsight reconstruction has long been banned. *See Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 227 USPQ 766 (Fed. Cir. 1985). In addition, even if there were

motivation to combine drkoop with Colon *et al.* and CenterWatch, the combined teachings would not teach or suggest each of the elements of claims 3 and 130-137.

Claim 3

The asserted motivation to combine these three references for the purpose of rejecting claim 3 is "the motivation of to [sic] assisting patents [sic] to participate in a clinical trial (page 2, lines 18-38)". Final Office Action at 24. First, the passage cited by the Examiner on page 2 of the reference does not say that its purpose is to assist patients to participate in clinical trials. The cited lines merely describe what drkoop planned to implement "[i]n a few weeks". *See* page 2, l. 18 et seq. No statement of purpose is included. The Examiner is therefore assuming that drkoop's planned system is intended to achieve that goal, even though the reference never states or suggests that is so.

Second, even if that assumption were valid, there is nothing in the reference to suggest that the goal was necessarily going to be achieved by the described system. The interactive pre-screening described in drkoop represents an extra step in a sometimes awkward process of enrolling in a clinical study to address a personal medical problem. The effect of such an extra step could just as likely have been to make enrollment more difficult. Thus, not only does the Examiner assume an unstated purpose to drkoop's planned implementation, the Examiner then assumes that the purpose would be successfully met and that it would motivate others to follow. Such speculation is hardly a proper basis for finding a motivation to combine references. *See In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991).

Finally, the Examiner's asserted motivation does not suggest the combination of these references. Of course assisting patients to participate in clinical studies is a desirable goal for those who work in this art. But such a general goal does not suggest the specific combination of these references. Indeed, if anything the fact that the Examiner was required to rely on three such disparate references suggests the patentability of the claims, as the art seems to have been consistently operating around the claimed invention, with each reference missing key components of Appellants' system. While the art may certainly desire to assist patients, it was the Appellants here who first conceived of a system that provides a single, Web-based interface

that provides information about various clinical trials, accepts enrollment information for those trials, automatically determines if the prospective patient is appropriate for the trials and then automatically notifies the patient of acceptance into the study. There simply is no suggestion in the art for such a technique.

Furthermore, even if there were a motivation to combine Colon *et al.*, CenterWatch and drkoop, and the combination were proper, Appellants submit that the combination does not render the pending claims unpatentable.

Claim 3 is directed towards a method for recruiting a person to participate in a clinical study comprising (a) presenting a website for the person to register with a database by providing registration and permission information; (b) registering the person with the database once registration and permission information is received; (c) automatically determining whether to provide the person with notice of a clinical study; (d) providing the person with notice of a clinical study; (e) automatically presenting a questionnaire associated with the clinical study to the person; (f) storing the answers submitted by the person in the database; and (g) accessing the answers to the questionnaire to determine whether the person qualifies to participate in a clinical study different from the given clinical study after step (f).

As noted above, neither Colon *et al.* nor CenterWatch teach or suggest, at the very least, steps (c), (d) or (e) of this method. drkoop does not solve the deficiencies of Colon *et al.* and CenterWatch. Initially, it is noted that drkoop speculates that in the future the cite may include questionnaires to pre-screen potential participants for a clinical trial. No clear statement is made as to how this speculative screening goal will be achieved. However, it appears from drkoop that the person responding to the to-be-implemented questionnaire of drkoop would have prior knowledge of the specific clinical trial for which they would like to be pre-screened for. See, for example, the paragraph starting on page 1, line 22, of drkoop:

> The center will give drkoop.com's 1.5 million monthly visitors access to information about clinical trials underway...It also will feature advanced on-line pre-screening to help identify the best candidates for further evaluation by physicians conducting *the* trials...

See also the paragraph starting on page 2, line 18, of drkoop:

> In a few weeks, interactive questionnaires to pre-screen potential participants will be added to the Clinical Trials Information Center. An individual's responses will be evaluated to determine if they meet *the* trial's basic criteria.

It is apparent from these passages that the person responding to the planned questionnaire of drkoop will have prior knowledge of the clinical trial, and that the site evaluates the persons appropriateness for that specific clinical trial. Therefore, drkoop does not solve the deficiencies of Colon *et al.* and CenterWatch because drkoop fails to disclose or even suggest steps (c) and (d) of claim 3, which require providing *notice* to a person of a given clinical study pursuant to an automatic determination of whether to provide that notice.

Claims 130-137

Although the Examiner rejected claims 130-137 in the same rejection and on the basis of the same prior art combination as claim 3, with respect to claims 130-137 he articulated a different motivation to combine Colon, CenterWatch and drkoop. In particular, in his treatment of claims 130-137, the Examiner asserts that a motivation to combine these references is "the motivation of increasing the likelihood that patients referred to a site are qualified to participate in the trial". Final Office Action at 24. Not surprisingly, claims 130-137 are directed to various types of screening questionnaires that, arguably, increase the likelihood that a patient is qualified to participate in a trial.

The fact that the Examiner has authored different motivations to combine the same references, with each motivation tracking the claim language at stake, strongly suggests that the Examiner's use of Appellants' disclosure as the guiding principle in rejecting the claims, rather than what was known or obvious to the art at the relevant time. Such analysis provides no basis for rejecting the claims. *See In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992).

The rejections are improper for other reasons as well. Colon *et al*'s system is operated by the study investigator, and there is a direct connection between the study investigator and the

clinical study center. But, in Colon *et al*'s system, the person or caregiver does not input the information themselves. CenterWatch takes a bulletin board approach, in which a person inputs basic information regarding him/herself and his/her disease condition and receives in return a long list of clinical studies being conducted for that condition. Neither of those systems would be concerned with prescreening patients at all. The purpose of CenterWatch is to provide a person with all of the clinical trial information available for their disease condition, even if they may not qualify for some or all of those clinical trials. Colon *et al.* on the other hand has no need of prescreening questionnaires, as the investigator/physician has already performed that function in person. Thus, the "motivation" relied on by the Examiner to combine drkoop with Colon *et al.* and CenterWatch would most likely strike one of ordinary skill in the art as adding nothing of merit to either Colon *et al.* or CenterWatch. There would be, therefore, no reason to combine them.

Moreover, drkoop does not solve the deficiencies of CenterWatch in view of Colon *et al.* Each of claims 130-137 ultimately depend on claim 2, and therefore include each of the limitations of claim 2, including steps (c), (d) and (e).In particular, the drkoop reference also fails to teach the provision of notice of a given clinical study pursuant to an automatic determination that such notice should be provided. Thus, even the unlikely combination relied on by the Examiner does not teach what Appellants claim.

Further, the limited disclosure of drkoop relied upon by the Examiner simply does not teach all the elements of claims 130-137. For example, while drkoop mentions "interactive pre-screening", page 2, line 27, claim 130 is directed to a pre-examination questionnaire and claims 131 and 134 are directed to screening questionnaires. Similarly, while drkoop states that his interactive pre-screening is intended to determine whether a patient meets "the trial's basic criteria", page 2, lines 20-21, claim 135 requires that the questionnaire be "protocol specific"; and claim 136 requires that the questionnaire be designed for screening of clinically appropriate persons. Thus, each of these claims defines over the limited disclosure of drkoop.

C. Rejection of Claims 138-151 Under 35 U.S.C. § 103(a)

(i) *The Examiner's Rationale*

Claims 138-151 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over CenterWatch in view of Colon *et al.* and further in view of drkoop.

In the final Official Action mailed June 3, 2003, the Examiner states that Colon *et al.* and CenterWatch do not disclose (1) presenting a screening questionnaire associated with a clinical study and (2) storing answers submitted by the individual in the database as required by these claims but that drkoop solves these deficiencies. The Examiner further contends that a combination of these references would have been suggested by "the motivation of increasing the likelihood that patients referred to a site are qualified to participate in the trial". Final Office Action at 26. Appellants respectfully disagree. In fact, many skilled in the art might be motivated to increase the referrals and send a broad swath of people directly to the sites for the sites to filter, rather than relying on a computer program, as opposed to a clinician, to screen patients.

(ii) *Summary of Appellants' Position*

The impropriety of the asserted motivation to combine these references is demonstrated above. The arguments previously set forth will not be repeated but are hereby incorporated by reference. Just as the Examiner's asserted motivations to combine references to support other rejections were improper with respect to other claims, so are they improperly used as a basis for rejecting these claims.

Similarly, because the claim language of dependent claims 130, 131, 134-137 corresponds to the language of dependent claims 141, 142, 145-148, and the rejection of all these claims are over the same combination of references, the arguments advanced above with respect to claims 130, 131, 134-137 are hereby incorporated by reference for claims 141, 142, 145-148, respectively.

D. Rejection of Claim 6 Under 35 U.S.C. § 103(a)

(i) *The Examiner's Rationale*

Claim 6 has been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over CenterWatch and Colon *et al.*, and further in view of "Pharmaceutical industry Embraces Clinmark Dotcom" (hereinafter Clinmark).

In the Official Action mailed on December 4, 2002, the Examiner acknowledged that CenterWatch and Colon *et al.*, even if taken together, do not disclose each of the steps of claim 6, specifically a step which requires providing a listing of information associated with a given clinical study in a personal library associated with a person or caregiver on the web site. However, the Examiner asserted that Clinmark discloses such a step.

In reply thereto, Appellants filed a Response, whereby the errors in the Examiner's rejection were discussed.

In the Official Action mailed on June 3, 2003, the Examiner responded by maintaining the rejection, arguing that and this combination was suggested by "the motivation of providing a forum for individuals with a common purpose about trends and exchange information [sic]." Final Office Action at 27.

(ii) *Summary of Appellants' Position*

The Examiner has asserted no proper basis for combining these references. It may be that "providing a forum for individuals with a common purpose to [gather and learn] about trends and exchange information" is a desirable goal, but that goal does not explain why one of ordinary skill in the art would be motivated to combine Colon *et al.*, CenterWatch and Clinmark. Indeed, Clinmark accomplishes that goal alone. See page 2. Why then would one be motivated to combine it with other systems? The answer, of course, is that one would not, unless one was reviewing Appellants' disclosure and wanted to find all the elements of the claims in the prior art. That, however, is the forbidden hindsight reconstruction and provides no basis on which to reject the claims. *See In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992).

Moreover, Clinmark does not solve the deficiencies of CenterWatch and Colon *et al.* when it comes to claim 6. Initially, it is noted that claim 6 is dependent on claim 5, which is in turn dependent on claim 2, both of which are patentable over the art of record.

Moreover, the Examiner misreads the claim. Claim 6 recites:

> 6. The method of claim 5, wherein step (d) further includes providing a listing of information associated with the given clinical study *in a personal library associated with the person or caregiver on the web site.*

(Emphasis added.) Thus, claim 6 is directed to providing a "personal library associated with" the person who has been given notice of a given clinical study.

Clinmark says nothing of such personal libraries. That system merely "offers electronic bulletin boards, job and RFP postings" and other types of postings relating to the industry. *See* page 2. There is no disclosure, express or otherwise, of providing a patient his or her own personal library on the site for any purpose, let alone for storing "a listing of information associated with the given clinical study" for which notice had previously been given. Thus, Clinmark, even if combined with Colon *et al.* and CenterWatch does not meet the elements of claim 6.

E. Rejection of Claims 13 and 14 Under 35 U.S.C. § 103(a)

(i) *The Examiner's Rationale*

Claims 13 and 14 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over CenterWatch and Colon *et al.* and further in view of Clinmark.

In the Official Action mailed on December 4, 2002, the Examiner argued that CenterWatch and Colon *et al.* disclose all of the steps of the methods of claims 13 and 14, except the steps of determining whether to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of an investigator, and providing the person or caregiver with answers by telephone, regular mail, facsimile, and other off-line sources. However, the

Examiner further argued that Clinmark purportedly disclosed these missing steps, and that it would be obvious to combine Clinmark with CenterWatch and Colon *et al.*

In reply thereto, Appellants filed a Response, whereby the errors in the Examiner's rejection were discussed.

In the final Official Action mailed on June 3, 2003, the Examiner responded by maintaining the rejection, but by failing to include any motivation to combine these references as to claim 13. *See* Final Office Action at 28.

(ii) *Summary of Appellants Position*

Claims 13 and 14 read as follows:

> 13. The method of claim 2, wherein a determination is made to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of an investigator associated with the study.
>
> 14. The method of claim 2, wherein the answers submitted by the person or caregiver are provided by telephone, regular mail, facsimile, and other off-line sources.

The Examiner agreed that the combination of CenterWatch and Colon *et al.* did not teach these claims. He nonetheless rejected them over Clinmark, CenterWatch and Colon *et al.*, arguing that one of ordinary skill in the art would have combined these references in order to "provid[e] information in a convenient manner for the requestor." Final Office Action at 29.

First, while Clinmark may provide information in a convenient manner (because it's an internet bulletin board), there is no explanation by the Examiner why that would suggest its combination with CenterWatch and Colon *et al.*. Indeed, since CenterWatch is also an internet bulletin board, the addition of Clinmark would appear to serve no purpose other than to meet the elements of Appellants' claims, an improper basis for its combination.

Nor would the combination meet the elements of these claims. Initially, as noted in more detail above, neither Colon *et al.* nor CenterWatch, either alone or in combination, teach or suggest each of the elements of claim 2, from which both claims 13 and 14 depend. Clinmark does not solve the deficiencies of Colon *et al.* and CenterWatch. For example, with respect to

claim 13, the specific paragraph cited by the Examiner for the proposition that Clinmark teaches making a determination of whether to provide notice "in accordance with a geographic location of an investigator associated with the study" was a sentence that contained the phrase "searched for oncologists in the United States."[2] Reading the entire sentence in context, however, leads one to a different conclusion. The relied upon statement was actually attributed to the director of clinical affairs of a Canadian laboratory who was searching for a study investigator. *See* page 2. The passage therefore discloses the use of the Clinmark system by a sponsor searching for a clinical investigator in the United States. Once the company identifies an investigator, the company notifies the investigator of the clinical trial they are conducting and starts a dialog to determine if that investigator would like to be associated with the clinical trial. Thus, the notification step in Clinmark is by a company to a clinical investigator. In contrast, the notification step of the claimed invention notifies a person or their caregiver of a clinical trial in accordance with a geographic location of an investigator associated with the study. Therefore, even if taken together, Colon *et al.*, CenterWatch and Clinmark do not disclose each of the elements of claim 13.

Regarding claim 14, the Examiner alleges that Clinmark discloses the submission of answers by the person or caregiver by telephone, regular mail, facsimile, and other off-line sources, citing a telephonic registration system. The answers referenced in claim 14, however, are answers to a questionnaire. *See* claim 2. There is nothing in Clinmark that suggests users can obtain a questionnaire, as claimed, and then report back the answers to that questionnaire via telephone.

[2] This passage was cited in the Official Action mailed on December 4, 2002. Page 17, line 13, of the Official Action mailed on December 4, 2002. The final Office Action maintained that rejection, but provided no further support for it. Page 13 of the final Official Action mailed on June 3, 2003.

F. Rejection of Claim 15 Under 35 U.S.C. § 103(a)

(i) *The Examiner's Rationale*

Claim 15 has been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over CenterWatch and Colon *et al.* and further in view of Larkin, Marilynn, "Where to find clinical trials on the Web" (hereinafter Larkin).

In the Official Action mailed on December 4, 2002, the Examiner acknowledged that CenterWatch and Colon *et al.*, even if taken together, do not disclose each of the elements of claim 15. Specifically, these two references fail to disclose a step of automatically determining, in accordance with the permission, registration and genetic information provided by the person, whether to provide the person or caregiver with notice of a given clinical study associated with a disease condition of interest to the patient. However, the Examiner purports that Larkin discloses this missing step of claim 15.

In reply thereto, Appellants filed a Response, whereby the errors in the Examiner's rejection were discussed.

In the Official Action mailed on June 3, 2003, the Examiner responded by maintaining the rejection.

(ii) *Summary of Appellants' Position*

Initially, and as demonstrated above, there is no suggestion or motivation in the art to combine Colon *et al.* and CenterWatch. Thus, this rejection must fail for that reason alone. Moreover, there is no motivation to further combine Larkin with Colon *et al.* and CenterWatch. Once again, the Examiner is clearly using Appellants' disclosure as a template for picking and choosing references in the prior art, that have no connection to each other, in order to meet all the elements of the claims. Such hindsight reconstruction has long been banned. *See Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 227 USPQ 766 (Fed. Cir. 1985). Thus, the Examiner has not indicated any motivation in CenterWatch, Colon *et al.* or Larkin to combine these references. Therefore, combining them is not proper.

Furthermore, even if there were motivation to combine each of these references, the combined teachings do not teach each of the elements of claim 15. Claim 15 is dependent upon

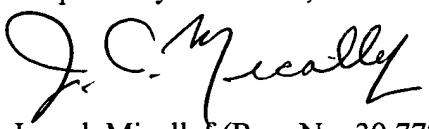
claim 2, and as noted in more detail above, Colon *et al.* and CenterWatch, even if taken together, do not disclose each of the elements of claim 2. Larkin does not solve the deficiencies of Colon *et al.* and CenterWatch, since Larkin does not disclose or suggest steps (c), (d) or (e) of claim 2. Furthermore, Larkin does not disclose or suggest modifying step (c) of claim 2 to include reference to genetic sequence information associated with a person registered in the database. Larkin says nothing about including reference to genetic sequence information. In the Official Action mailed on December 4, 2002, the Examiner specifically cites a section that says "the Epilepsy Foundation uses the web to recruit for its international *gene discovery* program." Larkin offers absolutely no information regarding the international gene discovery program and certainly does not teach including reference to genetic sequence information. Furthermore, the "recruitment" conducted by the Epilepsy Foundation is not sequence specific (as indicated by the fact that it is a "gene discovery program" and thus for the discovery of genes and their sequences not yet identified). Instead, when conducting a "international gene discovery project" one is searching for genes not yet genetically mapped, cloned and sequence, and therefore would recruit patients with epilepsy (and their relatives, afflicted and not afflicted by epilepsy) to conduct an investigation that will genetically map and clone genes associated with epilepsy.

In light of these remarks, it is clear that claim 15 is not obvious over CenterWatch in view of Colon *et al.* and further in view of Larkin.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse these Rejections and that the subject application be allowed forthwith.

Respectfully submitted,



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APPENDIX A

PENDING CLAIMS FOR 09/923,385

2. A method for recruiting a person to participate as a subject in a clinical study, comprising the steps of:

(a) presenting one or more web pages that allow the person or a caregiver associated with the person to register with a database by submitting registration information to the database, wherein the registration information includes at least a geographic location of the person, at least one disease condition of interest to the person, contact information, and permission information indicating whether the person or caregiver wishes to receive notice of one or more clinical studies;

(b) automatically registering the person or caregiver with the database upon receipt of the registration and permission information;

(c) after step (b), automatically determining, in accordance with the permission information and the registration information, whether to provide the person or caregiver with notice of a given clinical study associated with a disease condition of interest to the person;

(d) providing the person or caregiver notice of the given clinical study only if a determination is made in step (c) to provide such notice;

(e) automatically presenting a questionnaire associated with the given clinical study to the person or caregiver after step (d); and

(f) storing answers submitted by the person or caregiver in the database.

3. The method of claim 2, further comprising the step of:

(g) accessing the answers to the questionnaire along with other information in the database to determine whether the person qualifies to participate as a subject in a clinical study different from the given clinical study after step (f).

4. The method of claim 2, wherein the questionnaire includes criteria specific to a clinical study for determining whether the person is an eligible subject for the given clinical study.

5 .The method of claim 2, wherein steps (a) and (b) are performed during a registration visit by the person or caregiver to a web site associated with the one or more web pages, and step (g) includes notifying the person or caregiver of the given clinical study during a current or subsequent visit of the person or caregiver to the web site.

6. The method of claim 5, wherein step (d) further includes providing a listing of information associated with the given clinical study in a personal library associated with the person or caregiver on the web site.

7. The method of claim 2, wherein the notice provided in step (d) is sent by electronic mail from a web site associated with the one or more web pages to an e-mail address of the person or caregiver.

8. The method of claim 2, wherein the notice provided in step (d) is sent by regular mail to the person or caregiver.

9. The method of claim 2, wherein the notice provided in step (d) is communicated by telephone to the person or caregiver.

10. The method of claim 2, wherein a determination is made to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of the given clinical study.

11. The method of claim 2, wherein in step (c) a determination is made not to provide the person or caregiver with notice of the given clinical study.

12. The method of claim 2, wherein in step (a) the registration information includes whether the person is interested in clinical study information, whether the person is interested in new medical therapies, or whether the person is interested in participating in clinical studies.

13. The method of claim 2, wherein a determination is made to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of an investigator associated with the study.

14. The method of claim 2, wherein the answers submitted by the person or caregiver are provided by telephone, regular mail, facsimile, and other off-line sources.

15. The method of claim 2, wherein the step of automatically determining further includes reference to genetic sequence information associated with a person registered in the database.

129. A method for recruiting a person to participate as a subject in a clinical study, comprising the steps of:

(a) presenting one or more web pages that allow the person or a caregiver associated with the person to register with a database by submitting registration information to the database, wherein the registration information includes at least a geographic location of the person, at least one disease condition of interest to the person, contact information, and permission information indicating whether the person or caregiver wishes to receive notice of one or more clinical studies;

(b) automatically registering the person or caregiver with the database upon receipt of the registration and permission information;

(c) after step (b), automatically determining, in accordance with the permission information and the registration information, whether to provide the person or caregiver with notice of a given clinical study associated with a disease condition of interest to the person;

(d) providing the person or caregiver notice of the given clinical study only if a determination is made in step (c) to provide such notice; and,

(e) allowing the person or caregiver the opportunity to amend the registration information in the database during a subsequent visit to the web site.

130. The method of claim 2, wherein said questionnaire is a pre-examination questionnaire.

131. The method of claim 130, wherein said pre-examination questionnaire is a screening questionnaire.

132. The method of claim 130, wherein said pre-examination questionnaire is a pre-screening questionnaire.

133. The method of claim 2, wherein said questionnaire is a pre-screening questionnaire.

134. The method of claim 2, wherein said questionnaire is a screening questionnaire.

135. The method of claim 134, wherein said screening questionnaire is protocol specific.

136. The method of claim 2, wherein said questionnaire is designed for screening for clinically appropriate persons.

137. The method of claim 2, wherein said questionnaire requests information regarding inclusion/exclusion criteria.

138. A method for recruiting an individual to participate as a subject in a clinical study, comprising the steps of:

(a) presenting at least one web page to permit an individual to be registered with a database by indicating whether the individual wishes to receive notice of one or more clinical studies and registration information, wherein the registration information includes at least a geographic location, a disease condition of interest to the individual, and contact information;

(b) automatically registering the individual with the database upon receipt of the registration and indicating information;

(c) after step (b), automatically determining, in accordance with the indicating information and the registration information, whether to provide the individual or caregiver with notice of a clinical study associated with said disease condition;

(d) providing the individual notice of said clinical study;

(e) presenting a screening questionnaire associated with said clinical study; and

(f) storing answers submitted by the individual in the database.

139. A method comprising the steps of:

(a) presenting at least one web page to permit an individual to be registered with a database by submitting information indicating whether notice of one or more clinical studies is desired and registration information, wherein the registration

information includes at least a geographic location, a disease condition of interest, and contact information;

(b) automatically registering the individual with the database upon receipt of the registration and indicating information;

(c) automatically determining, in accordance with the indicating information and the registration information, whether to provide notice of a clinical study related to said disease condition;

(d) providing notice of said clinical study;

(e) presenting a screening questionnaire associated with said clinical study; and

(f) storing in the database answers submitted in response to said questionnaire.

140. A method of administering a database comprising the steps of:

(a) storing in a computer memory information indicating whether notice of one or more clinical studies associated with a particular disease condition is desired and registration information that indicates at least a geographic location, said disease condition of interest, and contact information; and,

(b) storing in said memory responses to a questionnaire associated with said notice.

141. The method of claim 140, wherein said questionnaire is a pre-examination questionnaire.

142. The method of claim 141, wherein said pre-examination questionnaire is a screening questionnaire.

143. The method of claim 141, wherein said pre-examination questionnaire is a pre-screening questionnaire.

144. The method of claim 140, wherein said questionnaire is a pre-screening questionnaire.

145. The method of claim 140, wherein said questionnaire is a screening questionnaire.

146. The method of claim 145, wherein said screening questionnaire is protocol specific.

147. The method of claim 140, wherein said questionnaire is designed for screening for clinically appropriate persons.

148. The method of claim 140, wherein said questionnaire requests information regarding inclusion/exclusion criteria.

149. A computer readable medium comprising computer executable instructions for performing the steps of:

(a) storing in a computer memory information indicating whether notice of one or more clinical studies is desired and registration information that includes at least a geographic location, a disease condition of interest, and contact information; and,

(b) storing in said memory responses to a screening questionnaire associated with said notice.

150. A computer readable medium comprising computer executable instructions for performing the steps of:

(a) providing information relating to at least one web page to permit an individual to be registered with a database by submitting information indicating whether notice of a clinical study is desired and a disease condition of interest;

(b) registering the individual with the database upon receipt of said information;

(c) determining in accordance with said information whether to provide notice of a clinical study related to said disease condition;

(d) providing notice of said clinical study;

(e) presenting a screening questionnaire associated with said clinical study; and,

(f) storing in the database answers submitted in response to said questionnaire.

151. A computer readable medium comprising computer executable instructions for performing the steps of:

(a) providing a web interface for registering an individual with a database by submitting information indicating whether notice of one or more clinical studies is desired and registration information, wherein the registration information includes at least a geographic location, a disease condition of interest, and contact information;

(b) determining whether to provide notice of a clinical study related to said disease condition;

(c) providing a web interface for submitting answers to a screening questionnaire associated with said clinical study; and,

(e) storing said answers in the database.